Induction of immune tolerance after spinal grafting of human ES-derived neural precursors

Grant Award Details

Induction of immune tolerance after spinal grafting of human ES-derived neural precursors

Grant Type: Transplantation Immunology

Grant Number: RM1-01720

Project Objective: To study immune tolerance and determine appropriate immunosuppression protocols to allow stem cell survival in a large animal model

Investigator:

Name:	Martin Marsala
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Neurological Disorders, Spinal Cord Injury

Human Stem Cell Use: Embryonic Stem Cell, iPS Cell

Award Value: $1,387,800

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title:	Induction of immune tolerance after spinal grafting of human ES-derived neural precursors
Public Abstract:	Previous clinical studies have shown that grafting of human fetal brain tissue into the CNS of adult recipients can be associated with long-term (more then 10 years) graft survival even after immunosuppression is terminated. These clinical data represent in part the scientific base for the CNS to be designated as an immune privilege site, i.e., immune response toward grafted cells is much less pronounced. With rapidly advancing cell sorting technologies which permit effective isolation and expansion of neuronal precursors from human embryonic stem cells, these cells are becoming an attractive source for cell replacement therapies. Accordingly, there is great need to develop drug therapies or other therapeutic manipulations which would permit an effective engraftment of such derived cells with only transient or no immunosuppression. Accordingly, the primary goal in our studies is to test engraftment of 3 different neuronal precursors cell lines of human origin once grafted into spinal cord in transiently immunosuppressed minipigs. In addition, because the degree of cell engraftment can differ if cells are grafted into injured CNS tissue, the survival of cells once grafted into previously injured spinal cord will also be tested. Second, we will test the engraftment of neuronal cells generated from pig skin cells (fibroblasts) after genetic reprogramming (i.e., inducible pluripotent stem cells, iPS). Because these cells will be transplanted back to the fibroblast donor, we expect stable and effective engraftment in the absence of immunosuppression. Jointly by testing the above technologies (transient immunosuppression and iPS-derived neural precursors), our goal is to define the optimal neuronal precursor cell line(s) as well as immunosuppressive (or no) treatment which will lead to stable and permanent engraftment of spinally transplanted cells.
Statement of Benefit to California:	Brain or spinal cord neurodegenerative disorders, including stroke, amyotrophic lateral sclerosis, multiple sclerosis or spinal trauma, affect many Californians. In the absence of a functionally effective cure, the cost of caring for patients with such diseases is high, in addition to a major personal and family impact. Our major goal is to develop therapeutic manipulations which are well tolerated by patients and which will lead to stable survival of previously spinal cord-grafted cells generated from human embryonic stem cells. If successful, this advance can serve as a guidance tool for CNS cell replacement therapies in general as it will define the optimal immune tolerance-inducing protocols. In addition, the development of this type of therapeutic approach (pharmacological or cell-replacement based) in California will serve as an important proof of principle and stimulate the formation of businesses that seek to develop these types of therapies (providing banks of inducible pluripotent stem cells) in California with consequent economic benefit.